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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,646	09/24/2003	Robert J. Steffan	WYNC-0809 (AM100977)	6797
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WOODCOCK WASHBURN LLP CIRA CENTRE, 12TH FLOOR 2929 ARCH STREET PHILADELPHIA, PA 19104-2891			ANDERSON, REBECCA L	
			ART UNIT	PAPER NUMBER
			1626	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/670,646	<b>Applicant(s)</b> STEFFAN ET AL.	
	<b>Examiner</b> Rebecca L. Anderson	<b>Art Unit</b> 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 August 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5 is/are allowed.
- 6) ☒ Claim(s) 1 and 6-16 is/are rejected.
- 7) ☒ Claim(s) 2-4 and 7-16 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Claims 1-16 are currently pending in the instant application. Claims 1 and 6-17 are rejected. Claim 5 appears allowable over the prior art of record. Claims 2-4 and 7-16 are objected.

### ***Election/Restrictions***

Claims 1-6 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 7-16 directed to the process of using an allowable product, previously withdrawn from consideration as a result of a restriction requirement are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement between groups I and II as set forth in the Office action mailed on 31 January 2006 is hereby withdrawn.** In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

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***Response to Amendment***

Applicants' amendment and arguments filed 7 August 2006 have been entered into the application. Applicants' amendment has overcome the objection to claims 1-6 as containing non-elected subject matter; has overcome the 35 USC 102 rejections of the claims; and has overcome the 35 USC 103 rejection of the claims. While applicant has requested the double patenting rejection to be held in abeyance, it is noted that the rejection is maintained as the rejection is proper. As applicants' product claims appear allowable over the prior art of record, the method claims 7-16 have been rejoined and are claims 7-16 are objected to as containing minor informalities; claims 7-9 and 13-15 are included in the provisional obviousness type double patenting rejection of record and claims 7-16 are rejected under 35 USC 112 1<sup>st</sup> paragraph as lacking enablement. As applicants' amendment to the claims has necessitated the new grounds of rejection, the office action is made FINAL.

***New Claim Objections***

Claims 2-4 are objected to as being dependent upon a rejected base claim, but would appear allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 7-16 are objected to because of the following informalities: Specifically, claims 7-16 as amended do not end in a period. Appropriate correction is required.

***Maintained Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

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unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 6 directed to an invention not patentably distinct from claims 1-7, 9-11, 18, 19, 22-24, 26, 31, 32 and 50 of commonly assigned US Patent Application 11/194263 (US Pre-Grant Publication 20060030612). Specifically, the conflicting claims

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claim compounds which generically encompass applicants' instantly claimed elected invention or positional isomers of applicants' instantly claimed elected invention and provide preferences towards applicants' instantly claimed invention or positional isomers thereof and also provide compounds which anticipate applicants' instantly claimed invention and provide specific compounds which are positional isomers of applicants instantly claimed invention.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned US Patent No. 11/194263 discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claims 1 and 6 and rejoined method claims 7-9 and 13-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being

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unpatentable over claims 1-7, 9-11, 18, 19, 22-24, 26, 31, 32, 33, 34, 38, 39, 40, 41, 44 and 50 of copending US Patent Application 11/194263 (US Pre-Grant Publication 20060030612). Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting claims disclose compounds which generically encompass applicants' instantly claimed elected invention or positional isomers thereof, for example, wherein in the conflicting claims R1 is CF<sub>3</sub> and R2 is phenyl substituted with O-C(O)R<sub>7</sub> or ortho or meta hydroxyl (see conflicting claims 1-7, 9-11, 18, 19, 22-24, 26 and 31) which corresponds to applicants' instant invention wherein R1 is arylalkyl, R<sub>9</sub> is trifluoromethyl, R<sub>6</sub>-R<sub>8</sub> are each hydrogen and the position equivalent to R<sub>4</sub> is OH, i.e. meta instead of para or OR<sub>10</sub> is OCOR<sub>11</sub> wherein R<sub>11</sub> is alkyl. The conflicting claims furthermore provide pharmaceutical compositions (see claim 50) and methods of use (claims 33, 34, 38, 39, 40, 41 and 44). Furthermore, specific compounds which anticipate applicants' instant invention or positional isomers are found in conflicting claim 32, see compound xj) 3-[2-benzyl-7-(trifluoromethyl)-2H-indazol-3-yl]phenyl acetate. Also, conflicting claim 32 claims specific positional isomers of applicants' instantly claimed invention, see compounds ad) and cd); 2-(2-benzyl-7-trifluoromethyl-2-H-indazol-3-yl)-phenol and 3-(2-benzyl-7-trifluoromethyl-2-H-indazol-3-yl)-phenol. Nothing unobvious is seen in substituting the known claimed isomer for the structurally similar isomer since such structurally related compounds suggest one another and would be expected to share common properties absent a showing of unexpected results. In re Norris, 84 USPQ 458 (1950). Therefore, since the conflicting claims of US Patent Application No. 11/194263 claim compounds which generically

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overlap with applicants' instantly claimed elected invention, provide preferences towards applicants' instantly claimed elected invention and also provide specific compounds which either anticipate applicants' instantly claimed elected invention or are positional isomers of applicants' instantly claimed elected invention, the claims 1 and 6 and 7-9 and 13-15 are therefore rejected under obviousness-type double patenting.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***New Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

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In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

***The nature of the invention***

The nature of the invention of claims 7-16 is the method of treating or inhibiting chronic inflammatory disease (claim 7), rheumatoid arthritis, spondyloarthropathies, osteoarthritis, psoriatic arthritis, juvenile arthritis (claim 8), inflammatory bowel disease, Crohn's disease, ulcerative colitis, indeterminate colitis (claim 9), psoriasis (claim 10), asthma, chronic obstructive pulmonary disease (claim 11), stroke, ischemia, reperfusion injury (claim 12), hypercholesterolemia, hyperlipidemia, cardiovascular disease, atherosclerosis, acute coronary syndrome, peripheral vascular disease, restenosis, vasospasm (claim 13), Alzheimer's disease, cognitive decline, senile dementia (claim 14), type II diabetes (claim 15), or sepsis (claim 16) or a method of lowering cholesterol, triglycerides, Lp(a), and LDL levels (claim 13). Furthermore, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

***The state of the prior art and the predictability or lack thereof in the art***

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

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It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of the above listed diseases, whether or not the disease is effected by a ligand of ER would make a difference.

Applicants are claiming methods which include the treatment of various diseases such as cardiovascular disease, stroke, inflammation, Alzheimer's disease, etc.

Applicants' claims are therefore drawn, for example, to the treatment of Alzheimer's disease. It is the state of the art that there is no known cure or prevention for Alzheimer's disease and that there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer's disease, Aricept, Exelon, Reminyl and Cognex, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. Memantine, which blocks excess amounts of glutamate treats late stage Alzheimer's disease.

([URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html](http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html)).

Furthermore, Layzer, Cecil Textbook of Medicine (article enclosed), states that "some degenerative diseases are difficult to classify because they involve multiple anatomic locations" (see page 2050). Alzheimer's disease has traditionally been very

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difficult or impossible to prevent or event o treat effectively with chemotherapeutic agents. See e.g., the Cecil Textbook of Medicine, 20<sup>th</sup> edition (1996), Vol. 2, wherein it is stated that “[t]here is no cure for Alzheimer’s disease, and no drug tried so far can alter theh progress of the disease” (pg. 1994).

In regards to the treatment of inflammatory disorders, enablement for the scope of treating inflammatory disorders generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process, which can take place individually in any part of the body. There is a vast range of forms that in can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no “magic bullet” against inflammation generally. Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilation and leaking of vessels, and recruitment of circulating neurophils. Chronic inflammation or “late-phase inflammation” is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. There are clusters of

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macrophages, which have stuck tightly together, typically to wall something off.

Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters. Otitis media is an inflammation of the lining of the middle ear and is commonly caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*. Cystitis is an inflammation of the bladder, usually caused by bacteria, Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasoacral duct and is caused by staphylococci or streptococci. Preseptal cellulites is inflammation of the tissues around the eye, and Orbital cellulites is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics. Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to accept any agent to be able to treat inflammation generally.

In regards to the treatment and prevention of various cardiovascular disorders, "Cardiovascular disorders" embrace a vast array of problems, many of which are contradictory to others. Thus, it covers hypertension and hypotension. It covers various types of arrhythmias; angina pectoris, the thrombotic symptoms of diabetes, atherosclerosis and hyperlipoproteinaemias, ischemic heart disease including

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congestive heart failure and myocardial infarction, stroke, and peripheral vascular disorders, such as deep-vein thrombosis, elevated blood levels of triglycerides, of total cholesterol or of LDL cholesterol, arteriosclerosis, peripheral vascular disease, cerebral vascular disease and pulmonary hypertension, migraine, cardiomyopathy, etc. Not one compound, let alone a genus of compounds, could possibly be effective against such disorders generally.

Stroke represents one of the most intractable medical challenges. Stroke is estimated to cause about 15% of deaths. Even those who survive normally suffer from persistent damage, including motor and speech disturbances and/or convulsions. Despite a tremendous effort to resolve these problems, cerebrovascular therapy as so far been limited to trying to prevent further damage in areas on the margins of the ischemic focus, this trying to maintain adequate perfusion in remaining intact areas, and thereby limit progressive infarction. This is generally done surgically. Standard pharmaceutical treatment, such as antiarrhythmics and antithrombotics don't get at the cause of the stroke or the damage caused, but are mostly done to insure adequate cardiac functioning.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by a ligand of ER one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims due to the unpredictability of the role an ER ligand and, for example, since it is known that there is no known cure for Alzheimer's disease and treatment protocols for Alzheimer's disease depend on the stage of the disease.

***The amount of direction or guidance present and the presence or absence of  
working examples***

The only direction or guidance present in the instant specification is the listing of diseases applicant considers as treatable by a ligand of ER on pages 1, 2 and 25-26. In vitro assay data is found on pages 17-18 with tables on pages 19-24. However, the disclosure does not provide how this in vitro data correlates to the treatment of the assorted list of disorders of the instant claims. There are no working examples present for the treatment of any specific disease or disorder. Further, there is no disclosure regarding how all types of the diseases having diverse mechanisms are treated. Receptor activity is generally unpredictable and a highly structure specific area, and the data provided of is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims. There is also no disclosure as to how the various types of cardiovascular, inflammatory, etc. disorders are treated or inhibited.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

***The breadth of the claims***

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The breadth of the claims is the method of treating or inhibiting chronic inflammatory disease (claim 7), rheumatoid arthritis, spondyloarthropathies, osteoarthritis, psoriatic arthritis, juvenile arthritis (claim 8), inflammatory bowel disease, Crohn's disease, ulcerative colitis, indeterminate colitis (claim 9), psoriasis (claim 10), asthma, chronic obstructive pulmonary disease (claim 11), stroke, ischemia, reperfusion injury (claim 12), hypercholesterolemia, hyperlipidemia, cardiovascular disease, atherosclerosis, acute coronary syndrome, peripheral vascular disease, restenosis, vasospasm (claim 13), Alzheimer's disease, cognitive decline, senile dementia (claim 14), type II diabetes (claim 15), or sepsis (claim 16) or a method of lowering cholesterol, triglycerides, Lp(a), and LDL levels (claim 13). Furthermore, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided. The disorders encompassed by the instant claims include, for example, inflammatory and cardiovascular disorders such as Alzheimer's disease and stroke, etc. some of which have been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same.

***The quantity of experimentation needed***

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all diseases would be benefited

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(treated) by a ligand of ER and would furthermore then have to determine which of the claimed compounds would provide treatment of which disease, if any.

***The level of the skill in the art***

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for of treating or inhibiting chronic inflammatory disease (claim 7), rheumatoid arthritis, spondyloarthropathies, osteoarthritis, psoriatic arthritis, juvenile arthritis (claim 8), inflammatory bowel disease, Crohn's disease, ulcerative colitis, indeterminate colitis (claim 9), psoriasis (claim 10), asthma, chronic obstructive pulmonary disease (claim 11), stroke, ischemia, reperfusion injury (claim 12), hypercholesterolemia, hyperlipidemia, cardiovascular disease, atherosclerosis, acute coronary syndrome, peripheral vascular disease, restenosis, vasospasm (claim 13), Alzheimer's disease, cognitive decline, senile dementia (claim 14), type II diabetes (claim 15), or sepsis (claim 16) or a method of lowering cholesterol, triglycerides, Lp(a), and LDL levels (claim 13) as a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention. (Only a few of the claimed diseases are

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discussed here to make the point of an insufficient disclosure, it does not mean that the other diseases meet the enablement requirements).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the method claims.

### **Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

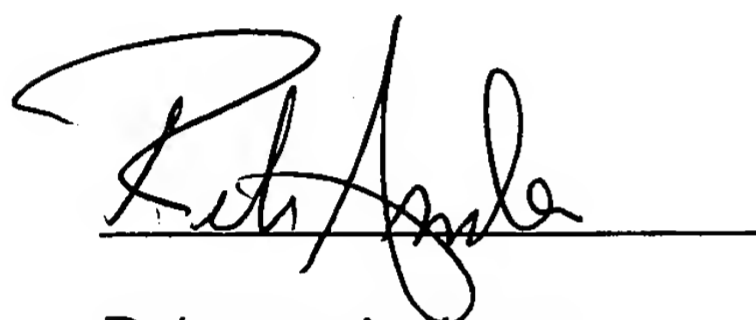
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Rebecca Anderson', is written over a horizontal line.

Rebecca Anderson  
Patent Examiner  
Art Unit 1626, Group 1620  
Technology Center 1600

27 November 2006